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ABSTRACT

Concerned with the increase in use of chewing tobacco and snuff, this brochure looks at the health risks of using smokeless tobacco. It presents five questions about smokeless tobacco use and provides answers to the questions developed by a consensus development conference on health implications of smokeless tobacco use convened by the National Cancer Institute, the National Institute of Dental Research, and the National Institutes of Health Office of Medical Applications of Research. Questions addressed include: (1) what are the current trends in the use of smokeless tobacco in the United States; (2) does the use of smokeless tobacco increase the risk of oral or other cancers; (3) does the use of smokeless tobacco increase the risk of peridontal disease or other oral and health problems; (4) what are the behavioral consequences of smokeless tobacco use; and (5) what issues regarding the health consequences of smokeless tobacco use require further research? The report notes that the human evidence that use of snuff causes cancer of the mouth is strong, while data are insufficient to come to any conclusions regarding the relationship of smokeless tobacco use to cancers at other sites. It concludes that use of smokeless tobacco is one of a number of health-endangering behaviors which frequently coincide, raising the potential for long-term and serious consequences. (NB)

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HEALTH IMPLICATIONS OF SMOKELESS TOBACCO USE

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Introduction

Smokeless tobacco includes both chewing tobacco and snuff. These products contain tobacco leaf and a variety of sweeteners, flavorings, and scents. In chewing tobacco, the leaf may be shredded (looseleaf), pressed into bricks or cakes (plugs), or dried and twisted into rope-like strands (twists). A portion is either chewed or held in place in the cheek or between the lower lip and the gum. The two categories of snuff, dry and moist, are made from powdered or finely cut tobacco leaves. In some countries, including historically the United Kingdom, dry snuff is sniffed through the nose, but in the United States both dry and moist snuff are used in the mouth or "dipped." A small amount (pinch) is usually held in place between the lip or cheek and the gum.

Although smokeless tobacco was widely used in the United States in the past, during this century its use has declined sharply. There is evidence that this trend has reversed and that smokeless tobacco is regaining popularity. Market data show increases in manufacturing and sales, especially in the category of moist snuff, and total annual sales of smokeless tobacco are now close to $1 billion. Reports from schools in different regions of the country indicate that smokeless tobacco—principally moist snuff—is being used by very young people, especially adolescent males.

Serious questions have been raised regarding health and behavioral effects of use of smokeless tobacco. Most notably, it has been linked to oral cancer. If smokeless tobacco use does produce adverse health effects, then its extensive use could have long-term public health consequences. It is important at this time that the available information be assessed, both to provide the scientific community with a synthesis of current knowledge and a framework

for further research and to provide the public with the information it needs to make informed decisions regarding use of smokeless tobacco.

To this end, the National Cancer Institute, the National Institute of Dental Research, and the National Institutes of Health (NIH) Office of Medical Applications of Research convened a consensus development conference on Health Implications of Smokeless Tobacco Use on January 13-15, 1986. After a day and a half of presentations by experts in relevant fields, a consensus panel including representatives of epidemiology, cancer, dentistry, psychology, pediatrics, psychopharmacology, education, and the public considered the evidence and agreed on answers to the following questions:

- What are the current trends in the use of smokeless tobacco in the United States?
- Does the use of smokeless tobacco increase the risk of oral or other cancers?
- Does the use of smokeless tobacco increase the risk of periodontal disease or other oral and health problems?
- What are the behavioral consequences of smokeless tobacco use?
- What issues regarding the health consequences of smokeless tobacco use require further research?

1.

What are the current trends in the use of smokeless tobacco in the United States?

The panel estimates that at least 10 million Americans have used smokeless tobacco within the past year, with 3 million of these users being less than 21 years old. Recent data indicate that significant proportions of teenage boys are current users, and the number of users in this age group is steadily increasing.

Detailed national data on trends in the use of smokeless tobacco are not currently available; however, there are indications of recent significant changes. One such indication is the amount of smokeless tobacco manufactured in the United States. Production declined steadily from 1930 until the late 1960's. Subsequently, there has been a resurgence of production, with a steady increase in total smokeless tobacco output of about one-third in the last 15 years; but in just the last 5 years the production of moist snuff alone, the form often used by youth, has increased by one-third.

The frequency of use of smokeless tobacco has only recently become a subject for national investigation. In 1985, a study based on a nationally representative sample revealed that 16 percent of males between 12 and 17 years of age had used some form of smokeless tobacco within the past year, and of these, about one-third used it one or more times per week. Males over 21 years of age use somewhat less, with use decreasing for older groups. These figures mask wide variations among subgroups. Only 2 percent of females use smokeless tobacco, and black and Hispanic males are intermediate-level users. Patterns of use appear to be similar in most of the country, but with the lowest use in the Northeast.

Some local studies have reported use by 30 to 40 percent of males in high school; even among third graders, 13 percent of males have reported use. One study showed that for males use increased with each grade. Significant use by kindergarten children also has been reported in some areas in one state. In a sample of colleges, about 20 percent of the males reported use of smokeless tobacco.

In the one local longitudinal study, covering 1976 to 1982, tobacco chewing doubled and snuff dipping tripled, with peak use among boys 12 to 14 years old. It is of interest that in some schools, the percentage of males reporting regular use of smokeless tobacco was higher than the percentage reporting regular use of cigarettes.

2.

Does the use of smokeless tobacco increase the risk of oral or other cancers?

Observations in humans provide convincing evidence for an increased risk of oral cancer as the result of use of smokeless tobacco. Data on humans are insufficient to determine whether cancers at sites other than the mouth and throat are related to smokeless tobacco use.

Human Data

With respect to human data, a North Carolina study of women provides the most compelling evidence of a role for snuff dipping in the causation of oral cancer. In this study, among nonsmokers the risk of oral cancer was 4.2 times greater for those who used snuff than for those who did not, and for those who were users over several decades the risk was much higher. These data are particularly striking in that (1) the cancer risks were greatest in those locations of the mouth where the snuff was placed; (2) the risk increased with increasing duration of snuff use; (3) factors such as diet, dental hygiene, alcohol intake, and cigarette smoking were found not to be responsible for the association between snuff and oral cancers; and (4) the risks were so large that it would be difficult to postulate alternative explanations for

the association between oral cancer and snuff other than a causal one.

These findings are supported by other epidemiological studies, primarily of the case control type, and by clinical case series. However, most of these studies did not specify the type of smokeless tobacco product, i.e., snuff or chewing tobacco. Thus, it seems prudent to recognize the carcinogenic potential of all smokeless tobacco products while acknowledging that the effect of snuff has been more fully documented.

Although this relationship has been most clearly demonstrated for elderly, rural women residing in the Southeastern United States, there is reason to believe that snuff would also be carcinogenic in women and men in all geographic locations. In fact, men using smokeless tobacco experienced a 3.9-fold increased risk for oral cancer in a study based on the Third National Cancer Survey. Young people, starting the use of snuff in grade school and continuing its use through adult life, are likely to experience comparable risks.

Our conclusion with respect to oral cancer is supported by multiple studies showing a relationship between oral cancer and chewing of betel quid containing tobacco in India and Southeast Asia. Furthermore, the conclusion is consistent with the judgment of a recent working group of the International Agency for Research on Cancer, which reported that the evidence associating snuff with oral cancer is "sufficient" to indicate a causal relationship.

Carcinogens in Smokeless Tobacco

Chemical analysis of various types of smokeless tobacco has revealed the presence of polonium-210, a radioactive alpha-emitter and known

radiation carcinogen, and representatives of two classes of powerful chemical carcinogens, the polycyclic aromatic hydrocarbons and the nitrosamines.

Of the 19 nitrosamines identified in smokeless tobacco, the carcinogenic nitrosamines presenting the highest concentrations are NNN and NNK, both of which are related chemically to nicotine. Snuff contains 1.6 to 135 mg per kilogram (mg/kg) of NNN and 0.1 to 14 mg/kg of NNK. Looseleaf and plug tobacco contain 0.2 to 8.2 mg/kg of NNN and 0 to 1.0 mg/kg of NNK. For comparison, U.S. foods and beverages may not contain more than 0.01 mg/kg of nitrosamines.

Both NNN and NNK readily produce cancer in rats and hamsters in organs such as the nose, trachea, esophagus, and liver. Benign tumors (papillomas) of the mouth are induced when NNN and NNK are applied directly to the mouth of rats.

Carcinogenesis Tests in Animals

Repeated experimental studies in animals have failed to provide adequate evidence that chewing tobacco, snuff, or extracts derived from them induce cancer.

Implications for Human Health

The risk of oral cancer in the United States is small for persons who do not smoke, drink alcoholic beverages, or use smokeless tobacco. The data considered here, however, raise the concern that regular users of snuff, especially children, may develop oral cancer later in life. The panel believes that the public should be warned that the use of smokeless tobacco, particularly snuff, increases the risk of oral cancer.

3.

Does the use of smokeless tobacco increase the risk of periodontal disease or other oral and health problems?

Evidence supports an association of smokeless tobacco use with gingival recession and oral leukoplakia, but there is insufficient evidence of an association with periodontitis or tooth decay. Other potential physical health hazards are essentially unexplored.

Gingival Recession, Gingivitis, and Periodontal Disease

Both case reports and studies of larger samples show an association of smokeless tobacco use with localized gingival recession (receding gums), especially where the tobacco is habitually placed. One study has reported a significant association of smokeless tobacco use with generalized gingivitis. Data currently are insufficient to support an association of smokeless tobacco use with generalized or advanced periodontal disease.

Tooth Decay

There are disparate data on whether smokeless tobacco use increases or decreases tooth decay. The absence of reliable data that take into account the diversity of smokeless tobacco products and the amount and bioavailability of contained sugars and fluoride may contribute to the lack of agreement among the few reports on this topic.

Leukoplakia

Several reports associate snuff use and, in at least one report, chewing tobacco use with the presence of white patches of the oral mucosa

clinically known as leukoplakia. Indeed, leukoplakia is a frequent concomitant of smokeless tobacco use. Although multiple studies describe the transformation of leukoplakia to malignancy within the range of 1 to 18 percent of patients over observation periods ranging from several months to 11 years, there are few data on whether snuff-associated leukoplakia per se undergoes similar frequencies of malignant transformation. The studies done to date probably have not been conducted for sufficient time or with sufficient numbers of long-term users to define the incidence of malignant transformation. Studies from India and Southeast Asia, involving different tobacco products and use patterns, suggest that the long-term risk for malignant change of smokeless tobacco-associated leukoplakia may be significant.

Other Health Risks

Blood levels of nicotine achieved by cigarette smoking, which are similar to those achieved by smokeless tobacco use, cause elevations of blood pressure, heart rate, certain blood lipids, and catecholamines. However, no direct epidemiological data are available on cardiovascular morbidity and mortality in association with smokeless tobacco use.

The complex array of constituents in smokeless tobacco presents a variety of potential health risks for the user as well as for the offspring of pregnant female users. In addition to nicotine, heavy metals such as lead and cadmium have been found in smokeless tobacco at levels that represent potential risks to the fetus and young child.

4.

What are the behavioral consequences of smokeless tobacco use?

The Effects of Nicotine

Tobacco produces psychological effects variously described as relaxing, arousing, and euphoriant. Over the past two decades, laboratory and clinical studies have indicated that these effects are mediated by nicotine and blocked by mecamylamine, a drug that competes for nicotine receptors in the brain. Tobacco use leads to a state of dependence in most regular users; this state is characterized by tolerance, physical dependence, and willingness to expend considerable efforts to maintain blood levels within a range of values bounded on the high side by toxic effects and on the low side by the onset of withdrawal symptoms. Blood levels achieved by smokeless tobacco use are similar to those of cigarette smoking. Nicotine self-administration patterns are very similar to those of other central nervous system stimulant drugs in both laboratory animal and human studies.

The abuse liability of a substance—the degree of its ability to gain control over the user—is correlated with the delay between administration and brain levels sufficient to engender a psychological effect. Because nicotine from smokeless tobacco is presumed to reach the brain more slowly than that from cigarette smoke, it might be hypothesized that smokeless tobacco would have lower abuse liability. However, in studies of teenagers who attempted to stop using smokeless tobacco, only a small percentage were able to do so, suggesting that tobacco by the oral route has substantial addicting properties. The continued use of smokeless tobacco even by those who experience serious

adverse health consequences attests to its addicting powers.

Addicted users of nicotine become tolerant to the drug; that is, despite experiencing initial unpleasant side effects (e.g., tremulousness, dizziness, and nausea), such users increase their dosage until it levels off at one that fulfills their need. Such users seek nicotine continually. Some users of smokeless tobacco use it even while sleeping.

The physical dependence associated with nicotine induces withdrawal symptoms when addicted users abruptly discontinue its use. Thereafter, ex-users often experience craving for nicotine and many become users again.

Other Behavioral Effects

Tobacco withdrawal produces increased irritability and decrements in several basic cognitive functions. These disruptive effects begin within hours of the last nicotine dose. Such cycles of intake and abstinence are typical of use patterns by youth in school and adults in many employment situations. Thus, the associated cognitive impairments could have adverse effects on academic and job performance.

Behaviors can become interchangeable based on their function to the individual. For example, current opinion is that some smokers are switching to smokeless tobacco because the latter is considered a safe alternative for maintaining their nicotine dependence. Other opinions are that young people using smokeless tobacco often switch to cigarettes. Use of smokeless tobacco in children is sometimes associated with the use of hard liquor, beer, wine, cigarettes, and marijuana.

Behavioral pharmacology and learning studies show that the determinants of the initiation,

maintenance, and reduction of substance use result from the interaction between biochemical and behavioral processes. For smokeless tobacco, nonbiochemical factors that are correlated and readily manipulable include advertisements about smokeless tobacco, influence from peers, parental acceptance of smokeless tobacco use, and a perception that smokeless tobacco may be less harmful than smoking tobacco.

5.

What issues regarding the health consequences of smokeless tobacco use require further research?

There is a pressing need for well-designed studies of:

a. Prevalence of smokeless tobacco use based on continuing national probability sample data, including type of product, age, sex, region, and concomitant cigarette smoking. In addition, longitudinal studies should be conducted.

b. Users and nonusers of smokeless tobacco products, to characterize better the prevalence and incidence of periodontal diseases, caries, leukoplakia, and cancer. These studies should identify, as far as possible, the nature and contents of products used, patterns and durations of use, concomitant use of other substances such as alcohol and smoking tobacco, and occurrence of viral infections. Where appropriate, they should use tissue biopsy as well as critical clinical and laboratory measurements.

c. Cancers of sites other than the mouth carried out in geographic areas with high rates of smokeless tobacco use.

d. Potential role of smokeless tobacco in cardiovascular disease and adverse outcomes of pregnancy.

e. Potential of users of smokeless tobacco to produce nitrosamines in vivo.

f. Research on the relationship between amounts of smokeless tobacco used and plasma levels of lead, cadmium, and other potential toxins.

g. Strategies for the development and evaluation of prevention programs, including school-based programs, taking into consideration regional, ethnic, age, socioeconomic, and other variables.

h. Development and evaluation of early intervention and treatment programs to reduce smokeless tobacco dependence, including a range of approaches based on pharmacological and behavioral treatments.

Specific populations that deserve special consideration include:

1. Elementary school, junior and senior high school, and college age young people.
2. Persons with specific risk or disease conditions, including malignancies, cardiovascular disease, women at risk for pregnancy.
3. Workplace- and industry-specific populations where elevated smokeless tobacco use is common.

Conclusions

Use of smokeless tobacco has a long history in the United States, but trends in recent years, in particular the increasing use of snuff by children and young adults, have led to concerns about possible health consequences. National data suggest that at least 10 million persons have used smokeless tobacco of one kind or

another within the past year. Patterns of use by age and sex appear to be similar across the country.

The human evidence that use of snuff causes cancer of the mouth is strong. Risk is particularly high for parts of the mouth were the snuff is usually placed. Data are currently insufficient to come to any conclusions regarding the relationship of smokeless tobacco use to cancers at other sites. Repeated experimental studies in animals have failed to provide adequate evidence that chewing tobacco, snuff, or extracts derived from them induce cancer. However, nitrosamines chemically related to nicotine occur at high levels in snuff and, generally, at lower levels in chewing tobacco. These compounds are highly carcinogenic in animals. The concentrations of nitrosamines in smokeless tobacco are far higher than the levels of these compounds allowed in any U.S. food or beverage.

Smokeless tobacco use increases the frequency of localized gum recession and leukoplakia where the snuff is usually placed, but evidence on its relationship to other diseases of the oral cavity is inadequate. The presence of lead in smokeless tobacco may pose a special risk for the developing fetus.

Use of smokeless tobacco releases nicotine into the bloodstream and produces blood levels of nicotine comparable to those produced by smoking tobacco. The primary behavioral consequence of regular use of smokeless tobacco is long-term nicotine dependence and its associated health risks.

Use of smokeless tobacco is one of a number of health-endangering behaviors which frequently coincide, raising the clear potential for long-term and serious consequences.

Members of the Consensus Development Panel Were:

Brian MacMahon, M.D., Ph.D.
Panel Chairman
Henry Pickering Walcott Professor of Epidemiology
Harvard School of Public Health
Boston, Massachusetts

Michael F. Cataldo, Ph.D.
Director of Psychology
John F. Kennedy Institute
Associate Professor of Pediatrics and Psychiatry
Johns Hopkins University School of Medicine
Baltimore, Maryland

Mary E. Collier
Chairman
Fairfax County School Board
Fairfax, Virginia

Robert J. Haggerty, M.D.
President
William T. Grant Foundation
Clinical Professor of Pediatrics
Cornell University Medical College
New York, New York

Theodore R. Holford, Ph.D.
Associate Professor
Department of Epidemiology and Public Health
Yale University School of Medicine
New Haven, Connecticut

Barbara S. Hulka, M.D., M.P.H.
Professor and Chairperson
Department of Epidemiology
University of North Carolina School of Public Health
Chapel Hill, North Carolina

Jonathan Leff
Editorial Consultant
Former Director
Consumer Reports Books
South Hero, Vermont

Dennis H. Leverett, D.D.S., M.P.H.
Chairman
Department of Community Dentistry
Eastman Dental Center
Rochester, New York

Peter N. Magee, M.B., F.R.C.P., F.R.C.Path.
Director
Fels Research Institute
Professor of Pathology
Temple University School of Medicine
Philadelphia, Pennsylvania

Sidney S. Mirvish, Ph.D.
Associate Director
Eppley Institute for Research on Cancer
University of Nebraska Medical Center
Omaha, Nebraska

Condict Moore, M.D.
Professor of Surgery
Director
Division of Surgical Oncology
University of Louisville School of Medicine
James Graham Brown Cancer Center
Louisville, Kentucky

Jason M. Tanzer, D.M.D., Ph.D.
Professor
Departments of Oral Diagnosis and Laboratory Medicine
University of Connecticut Health Center
Farmington, Connecticut

Travis I. Thompson, Ph.D.
Professor
Department of Psychology
University of Minnesota
Minneapolis, Minnesota

Members of the Planning Committee Were:

William J. Blot, Ph.D., (Cochairperson)
Chief, Biostatistics Branch
Chief, Analytical Studies Section
Division of Cancer Etiology
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

Gayle Boyd, Ph.D., (Cochairperson)
Research Psychologist
Office of the Director
Division of Cancer Prevention and Control
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

James P. Carlos, D.D.S., M.P.H.
Associate Director for Epidemiology and Oral Disease Prevention
National Institute of Dental Research
National Institutes of Health
Bethesda, Maryland

Jerry M. Elliott
Program Analyst
Office of Medical Applications of Research
National Institutes of Health
Bethesda, Maryland

John Grabowski, Ph.D.
Research Psychologist
Clinical and Behavioral Pharmacology Branch
National Institute on Drug Abuse
Rockville, Maryland

Stephen S. Hecht, Ph.D.
Chief
Division of Chemical Carcinogenesis
Naylor Dana Institute for Disease Prevention
American Health Foundation
Valhalla, New York

J. Michael Lane, M.D.
Director
Center for Prevention Services
Centers for Disease Control
Atlanta, Georgia

Brian MacMahon, M.D.
Henry Pickering Walcott Professor Epidemiology
Harvard School of Public Health
Boston, Massachusetts

Donald R. Shopland
Acting Director
Office on Smoking and Health
Department of Health and Human Services
Office of the Assistant Secretary for Health
Rockville, Maryland

Michael J. Bernstein
Director of Communications
Office of Medical Applications of Research
National Institutes of Health
Bethesda, Maryland

Ann Marrott
Public Affairs Specialist
Office of Cancer Communications
National Cancer Institute
National Institutes of Health
Bethesda, Maryland

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